

Exhibit A

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office via EFS-Web on 10/10/, 2006.

Autrey Brown
Autrey Brown

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Istvan Toth *et al.*

Application Number: 10/676,436

Filed: June 30, 2003

For: DELIVERY SYSTEMS

§
§
§
§
§
§
§
§

Confirmation Number: 9341

Examiner: Krishnan, Ganapathy

Group Art Unit: 1623

Attorney Docket No.: 36677.11
(formerly 4050.002900)

**STATUTORY DECLARATION OF WILLIAM ROY JACKSON
UNDER 37 C. F. R. § 1.132**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, William Roy Jackson, do solemnly and sincerely hereby declare as follows:

1. I am a Sir John Monash Distinguished Professor in the School of Chemistry at Monash University and have more than forty years of academic experience specifically in the field of Chemistry. I have published more than 350 scientific papers in peer reviewed international scientific journals and am currently active in this discipline. I also hold the title of Honorary Professor at Melbourne University, and serve as Chair of the Advisory Committee for the Victorian Institute of Chemical Sciences. A current copy of my *Curriculum Vitae*, including a selection of relevant publications, is attached hereto as **Exhibit WRJ1.**
2. I am a resident of Camberwell, Victoria, Australia, and am an Australian Citizen and British Subject. I do not have a financial interest in matters related to the above-referenced patent application. However, I am being/have been compensated for my time

in reviewing and studying the materials referenced herein and for executing the present declaration.

3. I have reviewed and understand the Specification, drawings, and claims of the above-captioned patent application and have also read and reviewed in detail the Official Actions issued by the U.S. Patent and Trademark Office (PTO) Examiner in charge of assessing the patentability of the referenced patent application, including dated July 14, 2005 and April 12, 2006.
4. I understand that the PTO Examiner in charge of assessing the patentability of the referenced patent application has rejected the claims of the pending application because the Examiner does not believe that the Specification adequately supports the breadth of the pending claims. I also infer from my reading of the Official Actions from the PTO that the Examiner appears to question whether the Patent Specification provides enough guidance for a trained scientist to be able to prepare and use the lipoamino acid- and lipoamino saccharide-based compounds disclosed in the patent application as carriers for therapeutically useful molecules.
5. I also understand from reading the Final Office Action dated April 12, 2006, that the Examiner believes that while the Specification is enabling for compounds of Formula I wherein the drug moiety is piperacillin, he concludes that it does not adequately provide enough guidance for one of skill in this art to be able to prepare and use the novel non-covalently linked lipoamino acid- and lipoamino saccharide-based compounds as carriers for therapeutically-useful drugs *other* than piperacillin.

6. Having considered the Specification in detail, and having reviewed all of the comments of the Examiner, I disagree with the conclusion drawn by the Office that the Specification does not provide sufficient teaching to enable one of skill in this field to prepare and use the lipoamino acid- and lipoamino saccharide-based compounds broadly as drug delivery agents as taught in the patent Specification. In particular, I disagree with the conclusion on page 3 of the Office Action that states "(o)ne of ordinary skill in the art will not extrapolate this to complexes comprising any drug since the example provided is not representative of all drugs and ionic complexes encompassed by the recitation of instant claim 1."
7. To the contrary, it is my belief that one of skill in the art *would*, in fact, "extrapolate" the teachings of the Specification, and would conclude that the lipoamino acid- and lipoamino saccharide-based compounds taught by the Specification would be useful in the delivery of a broad range of therapeutic molecules, including the many drugs that are taught in the Specification, and not just for the delivery of piperacillin.
8. In support of this conclusion, I refer to the Specification itself at page 70, wherein it describes the beneficial results achieved *in vivo* when using one of the disclosed liposaccharide compounds as a drug delivery molecule for increasing the oral absorption of an entirely different antibiotic, in this case, gentamycin sulfate. Likewise, on page 71, the Specification teaches that in addition to enhancing the oral absorption of gentamycin, the disclosed carrier molecules are also expected to be useful in providing enhanced delivery of other aminoglycoside antibiotics including, for example, neomycin, amikacin, tobramycin, and netilmicin.

9. Further in support of my position, I note the teaching outlined in Example 18 of the Specification. This section describes in detail the use of two of the claimed carrier molecules to improve the bioavailability of low molecular weight heparin. Figure 2 of the Specification summarizes these results. Furthermore, page 74 of the Specification also teaches that in addition to their use as delivery vehicles for heparin, the disclosed compounds are also expected to improve the delivery and bioavailability of "other heparinoid and sulfated or acidic oligosaccharides such as heparin, calciparine, enoxaparin, delteparin, nadroparin, danaparoid, fractionated low molecular weight heparin, fondaparinux, PI-88, hyaluronic acids, chondroitin sulfates, and physiologically acceptable salts thereof will be deliverable using the compositions of the present invention."
10. I further disagree with the Office's position on page 5 of the Action that concludes, "the instantly claimed invention is highly unpredictable since on (*sic*) of skill in the art cannot fully visualize or recognize the identity of the members of the genus." I disagree that one of skill in the art would be unable to "recognize the identity of" therapeutic drug molecules which could be delivered by the lipoamino acid- and lipoamino saccharide-based compounds taught by the Specification. Page 13 line 20 teaches the broad applicability of the claimed delivery vehicles, and notes that the therapeutically useful moiety ("D" in Formula I) may be "synthetic or natural peptides, proteins, mono- or oligosaccharides, sulfated antithrombotics or aminoglycosides. As stated above, exemplary aminoglycoside drugs are taught on page 71 of the Specification, while exemplary heparinoid drugs are disclosed on page 74 of the Specification.

11. It is my scientific opinion that the Applicants' patent Specification provides the requisite details, guidance, and information to direct a skilled artisan how to make and use the disclosed lipoamino acid- and lipoamino saccharide-based compounds as delivery agents for a variety of therapeutic compounds, including, for example, sulfated oligosaccharides, charged oligosaccharides, sulfated antithrombotics, and aminoglycosides.
12. I believe the teachings of the patent application when considered in concert with such exemplary general and specific knowledge in the art at the time the patent application was filed would be sufficient to provide a skilled person with the guidance required to make the drug delivery agents as described in the patent Specification, and to use them to deliver a variety of therapeutic drugs.
13. Finally, I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the *United States Code* and that such willful false statements may jeopardize the validity of the application or any patent issued thereon;

DECLARED at
Melbourne, Victoria, Australia
this 11th day of October 2006

)
)
)

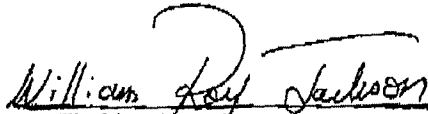
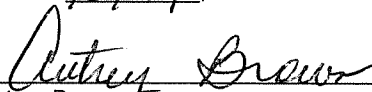

William Roy Jackson

Exhibit WRJ1

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office via EFS-Web on 10/12/, 2006.


Autrey Brown

CURRICULUM VITAE

NAME: William Roy Jackson

ADDRESS: **Business:** School of Chemistry
Box 23, Monash University, Victoria 3800
 Home: 30 Through Road, Camberwell, Vic 3124
 Phone (03) 9889 6583

DATE AND PLACE OF BIRTH:

27th February, 1935, Bacup, Lancashire, England, U.K.

CITIZENSHIP: British/Australian.

MARITAL STATUS:

Married, three children, born 1963, 1965 & 1967.

UNIVERSITY TRAINING:

B.Sc. Manchester (1st class Hons.) 1955.

Ph.D. Kings College, London University 1958.

D.Sc. London University, 1973.

APPOINTMENTS:

2004- Honorary Professor, Melbourne University

1995 – Sir John Monash Distinguished Professor, Monash University.

2003 - Chair, Advisory Committee, Victorian Institute of Chemical Sciences.
Professor (part time), Centre for Green Chemistry, Monash University.

2000 – 2002: Director, Centre for Green Chemistry, Monash University.

1973-99: Professor of Organic Chemistry, Monash University, (Head of Dept. 1992
- 1994).

1970-72: Reader in Chemistry, Queen's University of Belfast.

1962-70: Lecturer in Organic Chemistry, Queen's University of Belfast.

- 1959-62: Assistant Lecturer, Queen's University of Belfast.
- 1958-59: US Ethyl Corporation Postdoctoral Fellow at Oxford University with Professors E.R.H Jones, F.R.S. and M.C. Whiting.

AWARDS:

- 2003: Centenary of Federation Medal (for services to Applied Chemistry).
- 2002: Leighton Memorial Medal, Premier Award of the RACI.
- 1992: Baragwanath Award of Australian Institute of Energy (with Prof. F.P. Larkins).
- 1991: H G Smith Memorial Medal of R.A.C.I. for Research in Pure Chemistry.
- 1990: Fellow, The Australian Academy of Technological Sciences and Engineering.
- 1985: Sir Ian Wark Applied Research Medal of R.A.C.I. (with Prof. F.P. Larkins).
- 1982: Fellow, The Australian Institute of Energy.
- 1974: Fellow, The Royal Australian Institute of Chemistry.

UNIVERSITY APPOINTMENTS - INTERNAL:

- 2001: Chair, Review Committee, School of Music.
- 1995-98: Chair, Music Sub-Committee and Member of Performing Arts Committee, Monash University.
- 1993-95: Chair, Robert Blackwood Hall Management Committee, Monash University.
- 1992-94: Chair, Department of Chemistry.
- 1990-99: Elected member, Academic Board, Monash University.
- 1988-90: Member, Research Committee, Monash University.
- 1987-92: Member, Steering Committee, Professorial Board, University Research Committee.
- 1984-88: Chair, Monash University Open Day Committee.
- 1978-83: Chair, Union Board, Monash University.
- 1975-93: Director, Monash Blackwood Hall, Monash University.

1971-73: Member, Academic Council, Queen's University, Belfast.

UNIVERSITY APPOINTMENTS – EXTERNAL:

2005: Management Committee and Lecturer, Baeyer/United Nations, Eco-minds Forum, Manila,

Philippines.

2000: Dillon Lecturer, University of Queensland

1999: Chair, Review Committee, School of Mathematical and Physical Sciences, Murdoch University, Western Australia.

1998: Visiting Professor, Dyson Perrins Laboratory, Oxford University.

1997: Tasmanian Alkaloids Lecturer, University of Tasmania.

1996: Visiting Professor, University of Sassari, Sardinia, Italy.

1995: Japanese Government Distinguished Visitor, Hokkaido National Laboratory.

1993: Member, Review Committee, Department of Chemistry, Flinders University.

- 1992-97: Member, CSIRO Division of Chemicals and Polymers Advisory Committee.
- 1989: Invited lecturer, CNR Laboratories, Sassari and Florence, Italy; CNRS laboratories, Lyons and Paris, France. Guest of Pakistan council for Scientific and Industrial research and Indian Government Research Laboratories.
- 1983-84: Outside Study Program lecture tour of India, USSR, China, Japan and U.K.
- 1979: Visiting Professor, University of Canterbury, New Zealand.
- 1978: Study leave, University of Liverpool, with Professor C.W. Rees, F.R.S.
- 1967-68: Study leave, University of Texas, with Professor M.J.S. Dewar, F.R.S.

CONTRIBUTIONS TO COMMUNITY AND PROFESSIONAL ORGANISATIONS:

- 2005: Member, Future of Energy Research Committee, Victorian Government.
- 2004: Stranks Memorial Lecturer, South Australia.
- 2004: Keynote Speaker, Philippines Chemical Congress.
- 2002: Member, Science, Technology and Innovations Panel, Victorian Government.
- 2002: R.A.C.I. Tasmanian Youth Lecturer.
- 2001-present: Chair, R.A.C.I., General Administration and Membership Development and Marketing and Communications Committees.
- 2000-present: Chair, *Chemistry in Australia* Management Committee.
- 2000 - 01: President, R.A.C.I.
- 1995-present: Member, Editorial Advisory Committee, *Fuel Processing Technology*.
- 1993-94: Co-opted Member, Australian Research Council, Chemistry Panel.
- 1992-98: Member, Qualifications Committee, R.A.C.I.
- 1992-94: Member, Australian Research Council, Research Training and Fellowship Committee.
- 1991-96: Member, Biomedicine & Health Program, Australian Nuclear Science & Technology Organisation.

1990-91: Chair, R.A.C.I. Organic Chemistry Division.

1989: R.A.C.I. Tasmanian Youth Lecturer.

1985-88: Chair, R.A.C.I. (Vic.) Industrial Chemistry Group.

1983 – present: Assistant Australian Editor, *Fuel*.

1983 Member, Senate Enquiry into the deaths at the CSIRO Division of Applied Chemistry.

1983: Member, and Member of the Executive, Victorian Universities Admission Committee.

1982-1994: Member, Professional Accreditation Committee, R.A.C.I.

1980: President, R.A.C.I. Victorian Branch.

1979: R.A.C.I. Tasmanian Youth Lecturer.

1979: Vice President, R.A.C.I. Victorian Branch.

1978: Hartung Youth Lecturer, Victoria.

1972-1974: Member, Victoria University Schools Examination Board.

1969-1971: Northern Ireland Representative, Chemical Society.

1963-1972: Examiner and Chief Examiner, Northern Ireland G.C.E. Examination.

INVITED LECTURES:

Lectures at most universities in Australia and in academic, industrial and government laboratories in U.K., U.S.A., Germany, Canada, USSR, China, Japan, New Zealand, India, Pakistan, Israel, Italy, Ireland, Sweden, Hungary, France, Belgium and Spain.

Some recent Plenary Lectures:

- 2006: Invited Lecturer, International Symposium on Homogeneous Catalysis, South Africa.
- 2004: Philippines Chemical Congress, Iloilo City, Philippines.
- 2003: International Conference on Coal Science, Cairns.
- 2002: Plastics and Chemicals Industries Association (PACIA), Canberra.
- 2000: American Chemical Society, Honolulu.
- 2000: American Chemical Society, Washington.
- 1999: Indian Chemical Society, Calcutta.
- 1994: NATO Workshop on Organometallic Chemistry and Catalysis, Debrecen, Hungary.
- 1994: International Conference on Organic Synthesis, India.
- 1993: International Conference on Coal Chemistry, Banff, Canada.
- 1992: Euchem meeting, Alghero, Italy.

CONFERENCE ORGANISATION:

- 2002/2003: Chair of the Organising Committee, *12th International Conference on Coal Science*, Cairns, 2003.
Organising Committee, *International Conference on Homogeneous Catalysis*.
- 2001: Organising Committee, *International Conference for Coal Science*, San Francisco, USA.
- 2000: Divisional Organiser, *Pacificchem*, Honolulu, UAS.
- 1997: Co-chair, *Gordon Conference on Carbon-Based Materials*, Ventura, California.
- 1995: Australian Government Representative, *International Conference on Coal Science*, Oviedo, Spain.

- 1995: Divisional Organiser, *PacifiChem*, Honolulu, UAS.
- 1993: Australian Government Representative, *International Conference on Coal Science*, Banff, Canada.
- 1991: R.A.C.I. National Convention Organic Division, Monash University.
- 1990: Australian Government Representative, *International Conference on Coal Science*, Newcastle, U.K.

TEACHING:

- Involvement in all levels of undergraduate teaching.
- Assisted in the introduction of integrated first year courses in chemistry at Queen's and Monash.
- Specialist course for B.H.P. scientific and technical staff.
- Nominated as one of three "Most Respected Teachers of Chemistry" *Campus Review Weekly*, 1996.

RESEARCH INTERESTS:

Catalysis in Organic Synthesis

The development of new catalyst systems for organic chemical reactions with particular emphasis in obtaining good regio- and stereoselectivity. Many, but not all of the catalytic systems have been based on organometallic compounds. New asymmetric catalysts for the preparation of organic molecules with significant biological activity have been developed.

Structure and Reactivity of Coals

A major project has been carried out in collaboration with Prof. F.P. Larkins (University of Melbourne) into the structure and reactivity of coal with special emphasis on Victorian brown coals. A general structure for Victorian brown coal has been proposed and novel promoters for its reactions with carbon monoxide/water systems discovered. The interaction of brown coal with water has been analysed in terms of the structure of the coal leading to new drying methods.

New Materials

Development of new materials with applications in the areas of pharmaceuticals, controlled release of biologically active compounds and polymer attached liquid crystals for optoelectronic devices.

Green Chemistry

Design of new processes which, where possible, use renewable resources in reactions and which are environmentally friendly with a minimum of waste and energy expenditure. Current work involves a study of recoverable and reusable metal catalysts, replacement of

phosgene in polyurethane synthesis and preparation on non-addictive opioids from Australian poppies and a study of the influence of humic substances (including coal) in agriculture.

RESEARCH SUPERVISION:

Supervision or co-supervised 5 M.Sc. and 72 Ph.D candidates (59 at Monash and 13 at Queen's).

PUBLICATIONS (SUMMARY):

Papers in internationally recognised journals:	<i>ca.</i> 250 (in the area of synthetic chemistry) 91 (in the area of coal chemistry)
Reports to industry:	<i>ca.</i> 60
Patents (I.C.I., Amrad, Circadian):	12 (full)
Conference reports:	> 300

RESEARCH FUNDING:

Research funding ~ \$16 million has been attracted from applications involving Professor Jackson as Chief Investigator or Joint Chief Investigator from government and industrial sources both in Australia and overseas. Major sources have included the ARC (*ca* \$6 million) Amrad (\$1 million) Generic Technology Grant with Nufarm (\$1.8 million), Industry, including ICI/Orica, B.P. (\$3 million), Circadian (\$1 million).

Currently Professor Jackson holds an ARC Discovery Grant with Dr. A. Chaffee, an ORICA Strategic Research Grant with Dr. A. Robinson and has recently been involved in a successful bid for an ARC Centre of Excellence in Free Radical Chemistry and Biotechnology.

CONSULTANCIES:

Professor Jackson has acted as a consultant to several Australian companies including BHP and ICI Australia as well as smaller companies such as Pharmol Pacific. He is currently consulting with Avexa , Cortical Pty. Ltd. And the Victorian Government

He frequently serves as an expert witness in patent disputes.